III.—HISTOLOGY OF PERIPHERAL NERVES.

I. Leçons sur l'Histologie du Système Nerveux, par M. L. Ranvier. (*Lectures on the histology of the nervous system.*) Paris: F. Savy, 1878.

II. Axis Cylinder and Ganglionic Cell. By Hans Schultze. *Archiv f. Anatomie und Phys.*, 1878. Heft IV. and V., pp. 259.

III. Histology of Nerve Fibre and Axis Cylinder. By Th. Rumpf, in *Untersuchungen aus dem Phys. Institut der Universitaet Heidelberg.* (*Researches made in the Heidelberg Physiological Laboratory.* Edited by Dr. W. Kühne.) Heidelberg: Carl Winter, 1878.

I. The course of teaching pursued at the "College de France," at which L. Ranvier is Professor, differs from the plan of other institutes. It is intended not only to instruct students, but also to stimulate them to new researches. This merit is not the least important of Ranvier's work. This book brings the subject up to date in all its details, without, however, bearing the aspect of an encyclopedia. On the contrary, every new statement and every confirmation of the work of others bears the stamp of Ranvier's genius. The student, without previous knowledge of the subject, can not only follow profitably the work to the end, but he can also reproduce each result stated without previous preparation, such is the preciseness with which every method is detailed. The book besides abounds with suggestions; it is one of that rare kind which one cannot read without being stimulated to thinking. Necessarily there is a certain verbosity which may seem superfluous to the adept, but to which the work owes in part its easy reading and grace of style. The plates accompanying it render the book a work of art.

The introductory lecture treats of the evolution of the nervous system. In an amœba or a leucocyte we see an organism endowed with sensibility and motility. The globule, round and smooth when undisturbed, sends out prolongations and processes when irritated by contact of a foreign substance, but only on that side where it is touched, hence motility is evidently preceded by a sensation. The first *differentiation* into motor and sensory parts we find in the cells of the hydra as described by Kleinenberg. This animal has the shape of an open bag; the wall surrounding the internal cavity consists of three layers of cells called in analogy with embryonic nomenclature, ectoderm, mesoderm, and endoderm. Each cell of the outer layer is really continuous with a cell in the middle layer, the two together constituting the neuro-muscular cell of Kleinenberg. In the outer half resides the sensibility of the animal, while the inner part of the cell serves the purpose of motor elements. Further dif-

ferentiation of this apparatus gives gradually the schema of the nervous system of vertebrates.

Commencing hereupon the description of medullated nerve fibres, Ranvier combats the old view of the coagulation of myeline after death. From the end of a divided living nerve, examined in a drop of water, the myeline escapes slowly in curly streaks, and, after liberation, assumes the form of irregular globules without showing any signs of coagulation. This escape is not caused by the elasticity of the sheath of Schwann. This membrane folds itself over the axis cylinder, after the escape of the myeline, in such a manner as to show that it is neither very elastic nor stretched during the normal state. The escape is more likely due, according to Ranvier, to the hygroscopic properties of the myeline. The same phenomenon can be observed as well in a fluid less destructive to live cells than water, for instance, serum containing a trace of iodine. From the action of water the axis cylinder swells and becomes granulated.

Rumpf (III.) assigns a different cause for the escape of myeline. According to him the motive power is to be sought in the swelling of the axis cylinder by the action of water, which enlarging presses out the myeline. To prove this he dissolved the axis cylinders of fresh nerves by agents not altering the myeline, and on placing the specimen hereupon in water no escape of myeline occurred.—In the next place Ranvier studies the action of coloring agents. On placing a teased nerve into picrocarmine the coloration of the axis cylinder commences at the free end ; it proceeds also from the annular constrictions where the myeline is wanting. Where a fibre is accidentally bent in the form of a loop, the axis cylinder is pressed against the sheath of Schwann at the convexity of the bend displacing the myeline ; at such points also the coloration is more marked. From this can be deduced that the sheath of Schwann is permeable to solutions of crystallizable bodies—picrocarmine—while the myeline is not. On treating thin nerves while still in place with a solution of nitrate of silver—1 to 3 parts in 1,000—small crosses appear here and there after reduction of the silver by light. These correspond to the annular constrictions described some years ago by Ranvier. The short horizontal arm of the cross is a black line, indicating a thin layer of cement, interposed between the ends of the sheath of Schwann of two contiguous interannular segments. Hence, the sheath of Schwann of a fibre consists of as many segments as there are interannular divisions. The long vertical arm of the cross is formed by the axis cylinder blackened by the silver to a short extent on each side of the constriction. The agent evidently attacks the axis cylinder at the constriction, where no myeline exists, and extends its action a short distance either way. Higher powers of the microscope show that the axis cylinder is not blackened *in toto*, but that black cross-lines alternate with clear spaces—the striæ described by Frommann. Of these the author gives no further explanation.

The striæ of Frommann appear in a different light from the researches of Rumpf (III). In the same volume (Researches from the Heidelberg Laboratory) there is also a short note by Morochowetz on the action of silver, which confirms and extends Rumpf's remarks.

According to these observations the silver lines do not belong to the axis cylinder itself, but to the sheath of the axis cylinder —the internal horn-sheath—(which will be noticed in detail in a later part of this review). This can be shown by dissolving the axis cylinder after reduction of the silver—by which treatment the striæ are not altered. Rumpf succeeded also in coloring with silver nerves from which, by a method to be described hereafter, the axis cylinder had been removed during life, and still the silver striæ were produced. The black lines form a series of rings around the axis cylinder (or its sheath), which exceed slightly in diameter the thickness of the axis cylinder and sheath, as is apparent even in the original plates of Frommann (*Virchow's Archiv*, vol. 31). They correspond evidently to circular spaces around the axis cylinder filled with substances having an affinity for silver.

At the point of the annular constriction Ranvier describes a very regular bi-conical thickening of the axis cylinder. In his preparations this adhered to the axis cylinder when the latter was torn from the sheath of Schwann. Morochowetz, however, saw the same adhering in some preparations to the sheath of Schwann; in the latter case it had the appearance of a black circular disk forming a partition between the sheath of Schwann of two interannular segments, and perforated in the centre to give passage to the axis cylinder. Most probably this thickening or disk is identical with the layer of cement forming the short horizontal of the cross produced by nitrate of silver at the point of constriction.

Discussing the mode of employing osmic acid, Ranvier insists on keeping the nerve in its natural state of tension during the action of the agent. Nerves not stretched shrink and present altered appearances. He likewise insists that in the mounting in glycerine the latter fluid ought to be added very gradually if one wishes to avoid artificial deformations. Describing detailedly the annular constrictions, as seen after the action of osmic acid, he mentions that the sheath of Schwann is slightly dilated before its involvement in the constriction, hence a thickening of the coat of myeline at the ends of the segments. At the point of constriction the myeline is *always* interrupted. The apparently incomplete constrictions described by other authors are artefacts, as can be shown by compressing the nerve at some point while it is immersed in osmic acid. It is then found that the pressure displaces the semi-fluid myeline and causes it to rupture the attachment of the sheath of Schwann to the bi-conical thickening of the axis cylinder at the constriction of Ranvier. Hence the artificial appearance of continuity of the

myeline between two segments. Under the influence of osmic acid the myeline coagulates and becomes brittle; the hardened myeline breaks very easily, and at the point of rupture the sheath of Schwann can be more distinctly traced by the aid of any other method.

Each interannular segment possesses one nucleus, situated on the inside of the sheath of Schwann at or near its centre. It is surrounded by a thin coating of protoplasm, more voluminous in the young than in the adult. Very distinct preparations are obtained by coloration with picrocarmine after a short sojourn in osmic acid.

The appearances of cross-sections of hardened nerves are next described. During the hardening process the nerve is maintained in its normal state of tension. The axis cylinder of nerves hardened in chromic acid has a star-shaped appearance. This is an artefact; under the influence of chromic acid the myeline hardens in the form of globules, the convexity of which leaves its imprint on the contours of the soft axis cylinders. Other hardening agents do not produce this distortion. In the cross-section the axis cylinder is seen to be surrounded by a thin sheath which is not colored by carmine. The same appearance is found when an axis cylinder is isolated by teasing in osmic acid. This corresponds to the axial sheath described by Manthner, also Remak, Stilling and others. Klebs has asserted that the axis cylinder is surrounded by a periaxial free space. This, however, is an artefact; in reality there exists a sheath which shows no structure (except the rings developed by silver). In cross-sections differences are found between different fibres; this, however, depends on the place at which the nerve is cut. If the section passes through an annular constriction, the space between the axis cylinder and the sheath of Schwann is not filled with myeline, which, of course, *is* present when the section passes through any other point. But in many fibres seen in cross-section the myeline seems to be divided into two concentric rings by a clear line. This appearance is due to the segmental structure of the myeline as described by Schmidt (and independently of him by Lauterman and by Zawerthal). But this will be better understood after giving a *resumé* of Ranvier's view of the structure of medullated nerves.

Ranvier considers each inter-annular segment as the equivalent of a single cell, which he compares to an elongated adipose cell pierced in its centre by the axis cylinder. The sheath of Schwann he considers as the cell membrane, the contents of which are the nucleus, situated excentrically, and myeline. Between cell membrane and myeline he claims the existence of an extremely thin layer of protoplasm, as it is also found in the fat cell. This protoplasmic layer, lining the sheath of Schwann, passes over to the axis cylinder at the point of constriction, and thence returns to the other end of the segment as the sheath of the axis cylinder. From the latter protoplasmic partitions pass

in an oblique direction to the protoplasm lining the sheath of Schwann, and the portions of myeline separated by these partitions constitute the segments of Schmidt. In the isolated nerve fibres these segments of Schmidt appear as cylinders of unequal length, one end being conical and fitting into the corresponding concave end of the adjoining cylinder. If a cross section be made through the junction of two myeline segments, the protoplasmic partition is seen as a clear ring, with a concentric ring of myeline on either side of it.—This view appears original and striking, but Ranvier himself does not consider it more than a hypothesis. It is true that the supposed protoplasmic nature of this lining layer has only been demonstrated around the nucleus, but the protoplasm is ordinarily also not visible in the circumference of adipose cells, unless swollen from œdema.

Much light has been thrown on the chemistry and structure of these lining layers by the researches of Kühne and Ewald. ("Die Verdauung als histologische Methode." *Verhandl. d. Naturh. med. Vereins zu Heidelberg.* Sep. Abdr. Nov., 1876.) Although they were published before R.'s book was completed, they are not quoted by him.

These authors dissolved the myeline of peripheral nerves and sections of the spinal cord in boiling alcohol and ether, and digested hereupon the remnant with a solution of *trypsin* (pancreatin). There remained after digestion two sheaths, one within the other, with a trellis-work of the same material uniting them. The inner sheath is evidently the tunic of the axis cylinder, while the outer sheath encases the myeline, separating it from the sheath of Schwann.

The material of which these "horn-sheaths" are composed is called by Kühne "neurokeratine." With the aid of the same method E. and K. also discovered that there exists on the outside of the sheath of Schwann a thin coating of longitudinal collagene fibres. The sheath of Schwann itself is dissolved by trypsin.

Further details resulting from these investigations have been furnished by Rumpf. Instead of ether and boiling alcohol, hot chloroform can equally well be used to dissolve the myeline in order to demonstrate the horn-sheaths and trabeculæ. Although visible after this procedure alone, they gain in distinctness by subsequent digestion of the axis cylinder by trypsin. Another method is furnished by dissolving myeline and axis cylinder in glycocholate of sodium (bile). Perhaps the least objectionable procedure consists in the expulsion of the myeline by the swelling of the axis cylinder from the action of distilled water. Prolonged maceration in water (for twenty-four hours) finally *dissolves* the axis cylinder entirely. The two horn-sheaths are then seen as concentric tubes, one within the other, the outer one being quite distinct from the sheath of Schwann. Thick trabeculæ pass at intervals from one to the other, in an oblique direction. Usually there are three trabeculæ radiat-

ing at once level from the inner sheath, thus forming a series of incomplete partitions which divide the myeline into the segments of Schmidt. The statements of Ranvier as to the existence of a lining of the sheath of Schwann continuous with the sheath of the axis cylinder, are hence supported by these preparations. Even his assertion that this system of sheaths is protoplasmic in nature is not disproven. The sheaths, as demonstrated by maceration in water, do not consist alone of neurokeratine, but contain besides albuminoids. In proof of this they can be colored by Millon's reagent. Furthermore, they become reduced in thickness by digestion with trypsin, which dissolves the albuminous portion. The inner horn-sheath covers the axis cylinder continuously, passing with it through the constrictions. The outer sheath is also uninterrupted in its course, but constricted together with the sheath of Schwann at the level of Ranvier's annular constrictions. The myeline is undoubtedly interrupted at this point, probably by the disc of cement which becomes blackened when treated with silver. This bar, however, of cement can easily be forced by violence.

Rumpf has made some important researches in the chemical nature of the axis cylinder. By an intense red coloration with Millon's reagent, he demonstrated positively the albuminoid character of this structure. The fresh axis cylinder is soluble in distilled water, bile, and still more so in a 0.1 per cent. solution of potassic hydrate. By the action of alcohol, however, it is coagulated, and in this state insoluble in the above reagents. Coagulation is also produced by a temperature of 50 to 52° C. (nerves of the frog).

In order to search for myosin—the albuminoid of muscles—in the axis cylinder, nerves were placed into solutions of NaCl. of the strength of 5 to 10 per cent., in which myosin is soluble. Such fluids, however, did not dissolve the axis cylinder, but on diminishing the concentration the astonishing observation was made, that water containing less than one per cent. of salt removed the axis cylinder completely. Hitherto a 0.75 per cent. solution of NaCl. had always been considered an indifferent fluid for nerves! Nevertheless, this dissolves the axis cylinder completely within 72 hours without producing any other changes in the remaining structures. Weaker solutions produce the same result still faster, but cause the axis cylinder to swell in the first place and hence force out the myeline. This unexpected observation induced Rumpf to test the solvent action of lymph, which contains the same percentage of salt as the hitherto supposed "indifferent" fluid. To his astonishment he found *the axis cylinder of excised frog's nerves completely dissolved in frog's lymph* within three days! Further experiments of Rumpf relating to the persistence of the axis cylinder during life will be related further on.

The fibrillary structure of the axis cylinder, as described by Max Schultze, is not mentioned by Ranvier in this place. Later

on, however, he declared himself partisan of that theory, which, although he found no evidence of it in ordinary nerves, he could satisfactorily prove in some other cases. In the central end of divided nerves (Vol. II., p. 30) the axis cylinder swells—becomes hypertrophied as R. calls it—and in this state shows a distinct striation—an appearance which could only be caused by a bundle of fibrils. Another instance of distinct striation was found by Ranvier in the nerves of the electric organ of the torpedo (Vol. II., p. 125). In this organ the medullated nerves present a vague striation, their unmedullated twigs, however, are seen distinctly to consist of fibrils. In this instance the branches together are often more voluminous than the axis cylinder of the nerve fibre from which they arise. As a cause, Ranvier observed distinctly that the ultimate fibrils of which these branches consist pass from one branch into another without entering the larger fibre from which the branches arise. Thus there is formed a system of loops connecting the different nerve terminations.

Positive demonstration of the fibrillary structure of the axis cylinder was furnished by Hans Schultze (II.). Fresh nerves observed in iodized serum as well as in other fluids, show a decided striation of the axis cylinder. A particularly good object was found in the spinal roots of the frog. The most conclusive preparations were obtained by the use of very dilute solutions of osmic acid or nitrate of silver. In these the end of the axis cylinder protruding beyond its sheath seems to split up like a camel's hair pencil into separate fibrils. By careful adjustment of the focus the fibrillæ could be traced along the course of the axis cylinder. The plates accompanying Schultze's article are perfectly convincing—provided they are not exaggerated. Schultze claims that the fibrils are imbedded in a granular mass. The same appearances he could also trace in the transparent tail of the living embryonic salamander.

Ranvier has also examined living nerves in the lungs of the frog distended by the apparatus of Holmgren. Under these circumstances no fibrillation was seen by him. But he strongly insists on the fact that the living nerve thus displayed, shows the difference between the axis cylinder and myeline, as well as annular constrictions and the segments of Schmidt, in a perfectly unequivocal manner.

In the description of non-medullated fibres (Remak's fibres) Ranvier points out the confusion of authors in not distinguishing between connective tissue fibrillæ and Remak's nerve fibres. Both show a longitudinal striation; but the former have the appearance of a bundle of wavy hairs, running parallel, while the latter form a net-work with elongated meshes of anastomotic tendrils of unequal thickness. The thickness, however, depends on the number of ultimate fibrils of which the coarser fibres are composed. Each ultimate fibril has a nucleus on its surface with a thin protoplasmic coating. No sheath can be demonstrated around the fibres. Remak's fibres are colored orange by piero-

carmine, which does not stain connective tissue fibres. But the most certain test for non-medullated nerve fibres is maceration in bichromate of ammonium, which produces such numerous vacuoles, as to give the fibres the appearance of pearl strings.

The description of the connective tissue of nerves is preceded, as indeed are all chapters, by a short but judicial historical review. Like his immortal master, Claude Bernard, Ranvier does not content himself with simply quoting and throwing overboard the results of authors whom he is forced to contradict, but seeks the cause of their errors in the conditions of their experiments. Isolated nerve fibres in their course through muscles are seen to be enclosed by a sheath, which Ranvier calls after its discoverer, the sheath of Henle. It seems to be structureless, but is lined on its internal surface by endothelial cells, not forming a continuous layer. Besides these cells two other kinds can be recognized, viz., independent connective tissue cells, situated far apart between the sheaths of Schwann and of Henle, and flat connective cells on the outside of the sheath of Henle. Small nerve-branches, containing several fibres, possess a similar sheath, in the inside of which, however, the endothelial cells form a continuous layer. As the trunks increase in size, their sheath is transformed into a structure, called by Ranvier "lamellar" sheath. In its description Ranvier becomes quite polemical. Robin is charged with an incorrect, in fact, imaginary description, while Axel Key and Retzius, who agree with our author, are accused of ignoring R.'s priority, since in 1872 he published his first article on the subject, an article which remains undisputed.

The "lamellar" sheath consists of a series of thin, concentric layers, varying in number with the thickness of the nerve. Each layer is formed of a trellis of connective fibres, with some elastic fibres woven in and lined on both surfaces with endothelial cells. Each layer is perforated by irregular windows. Trabeculæ pass from one layer to another, so as to give the whole considerable strength. From the centre (innermost layer) to the periphery the layers increase in thickness, until they finally blend with the areolar tissue surrounding the nerve trunk, the perifascicular connective tissue, as it is called by Ranvier. Under the name intrafascicular connective tissue, he designates the areolar frame of the trunk itself. The inner layers of the lamellar sheath send irregular partitions into the trunk; from these secondary branches proceed and subdivide further. The ultimate elements of which these are composed are connective tissue fibres and flat cells. Each nerve fibre is finally surrounded by a sheath of longitudinally arranged connective tissue fibrillæ. This description corresponds with the results obtained by Ewald and Kühne with the digestion method.

The vessels of the nerve trunks pass along in the sheath and connective tissue partitions to the inside of the trunk. Around the nerve fibres the capillaries form a characteristic net-work with elongated meshes. The capillaries have the shape of loops, from

the convexity of which other capillaries arise. They are covered by an adventitial sheath consisting of flat cells. Lymph-vessels do not exist in nerve trunks; they are only found in the perifascicular tissue. In the trunk the lymph finds its way, as can be shown by injections, between the interspaces of the areolar framework and of the lamellar sheath.

To illustrate some points in the nutrition of nerves, an interesting experiment is next shown by Ranvier. In a living rabbit the sciatic nerve is exposed, and the wound filled with pure tepid water, which is repeatedly renewed. In the course of twenty minutes, that portion of the nerve which has been bathed in water has lost both excitability and conductility. Examined after treatment with osmic acid, it is found that the water has entered at the constrictions and crowded back the myeline ; the dilated pocket of the sheath of Schwann at the ends of the segment contains a fluid, in which fine granulations are suspended. The axis cylinder is swollen, as are also the partitions of Schmidt. If a 0.5 per cent. solution of NaCl. is substituted for the water the nerve does *not* lose its properties, even after 5 hours. Nevertheless, the microscope reveals the same changes, with the interesting addition of a distinct striation of the axis cylinder. The pure water must hence have produced invisible changes besides these, to account for the paralysis. The action of water, moreover, is permanent; a nerve destroyed by it does not recover its properties, but degenerates as after section.

Ranvier's description of the degeneration of divided nerves is, no doubt, the most complete article on the subject. Bakowiecki has recently maintained, that previous attempts to prevent degeneration by a suture of the divided nerve failed on account of the material employed. In his own experiment he claims to have obtained anatomical as well as physiological union by the use of a catgut suture. Ranvier, however, denies the accuracy of these statements, on account of a total want of success in his own experiments.

The rapidity with which the peripheral segment of the divided nerve loses its properties depends on the energy of life. The time is slightly shorter in young, than in older animals. While in the cold-blooded frog the nerve retains its motility for thirty days, and in the sluggish plagiostoma even more than six weeks, the peripheral stump becomes unexcitable within four days in dogs, three in pigeons, and two in rabbits. Ill-health also retards the time. The animal which has suffered from the wound necessary for the section of one nerve, retains in this state the properties of a second nerve, now divided, a few hours longer than when normal. Some experiments, however, to retard the time by bleeding the animals, did not succeed.

In order to avoid any confusion between the histological changes of degeneration and the cadaveric alterations of nerves, Ranvier devotes a short paragraph to the details of the latter. Twenty-four hours after death the myeline has receded slightly

from the ends of the interannular segments, and the sheath of Schwann here encloses a clear fluid. Beyond this, however, the nerve appears unchanged, and remains so for about 12 days. It is only after the lapse of this time that the myeline becomes opaque and charged with fatty granules.

The peripheral stump of a nerve examined within one hour after its division, shows the myeline escaping from the point of section. The myeline is swollen, opaque and granular in appearance. Engelmann recently claimed, that this process did not extend beyond the first constriction in either peripheral or central stump. Guiseppe Colasanti (*Arch., f. Anat.* Heft III. and IV., 1878, p. 206,) confirms this statement. According to his description the entire nerve—as far as the first constriction—consists of a strongly refractive, apparently homogeneous mass. He proposes to call this alteration, traumatic change of divided nerves.

Ranvier admits this limitation of the process in frogs, but claims that in mammals it does extend beyond the first constriction ; yet he does not describe any further details. Besides this alteration of the nerve fibres, red and white blood globules are found at the point of section. The leucocytes are infiltrated with myeline and fat. From analogous experiments on the omentum of Guinea-pigs, Ranvier admits that the flat cells of the intrafascicular connective tissue can be transformed into leucocytes.

Twenty-four hours after the section changes begin in the peripheral portion of the nerve. The nuclei of the interannular segments become hypertrophied and their nucleoli more marked. The protoplasm surrounding the nucleus is also swollen and can be seen to line the sheath of Schwann in its entire extent.

After the lapse of fifty hours these changes have progressed (in the rabbit). The intense swelling of the protoplasm now displays the protoplasmic nature of the partitions of Schmidt. By their enlargement the myeline becomes divided into fragments. At other points, however, especially around the nucleus, the protoplasm forms projections, which cut through both myeline and axis cylinder, and finally, fill completely the sheath of Schwann. The myeline continues to divide still further, until the whole nerve tube becomes filled with minute drops, partly myeline, partly fat. The oleaginous portion of the myeline is changed partly into a soluble soap, which is absorbed by the protoplasm, and redeposited in its interior in the form of oil globules.

What becomes of the axis cylinder? This question has been variously answered by different observers ; indeed the solution is very difficult. The coloration of the axis cylinder is not obtained easily on account of the impermeability of the myeline to coloring fluids. The best results were obtained by Ranvier by maceration in bichromate of ammonium. This hardening fluid produces fissures in the myeline, through which the coloring agent—picrocarmine—can reach the axis cylinder. The latter is now seen—divided into fragments of unequal length, by an

occasional projection of protoplasm. The fragments are often spiral in shape, evidently from pressure of the segmenting myeline.

About the fifth day the nuclei begin to multiply. The nucleolus enlarges in the first place, gets the shape of a figure 8 and then divides. Hereupon the nucleus undergoes the same changes. The two nuclei thus created subdivide into four, and so on. This multiplication of nuclei ceases, however, within some days.

About the 12th day the nerve tube is filled with drops of myeline, nuclei and an intermediate substance. The myeline drops were not stained uniformly by osmic acid, some of them being scarcely colored. Since the dark coloration produced by osmic acid depends on its combination with fats, it is probable that these have been dissolved out of the colorless drops. The intermediate substance consists of protoplasm, which appears striated longitudinally.*

From this time onward, until about the seventy-second day, the nerve changes scarcely any in appearance.

The unmedullated nerve fibres also undergo certain changes after section of the nerve. Their nuclei enlarge and become filled with several nucleoli. Some nuclei have the shape of a figure 8. As to their multiplication, however, Ranvier is silent. In the interior of the fibres small vacuoles appear. These are replaced within a few days by fat-granules. Myeline drops are never seen.

As regards the connective tissue of nerves, no change is found in the fibres. The flat cells, however, enlarge, or at least become more distinctly visible, and become studded at first with vacuoles, and subsequently with fat granules. Myeline drops are found in their interior only at the point of the section. Later, about the twentieth day, the cells attain a globular shape and are infiltrated with some substance colored uniformly bluish-grey by osmic acid. The endothelial cells of the vessels undergo the same changes.

In short, we can say that the primary changes in the peripheral segment of a divided nerve consist in the growth of all the protoplasm contained, viz., protoplasm of interannular segment, of the connective tissue cells and of the vessels. At the same time it becomes infiltrated with fat granules, evidently derived from saponification of the fatty parts of the myeline. The destruction of the axis cylinder and myeline are only secondary. The loss of function coincides with the fragmentation of the axis cylinder by the encroaching protoplasm.

Meanwhile changes of a different nature have occurred in the

* As regards the behavior of the "horn-sheaths" during the degeneration of peripheral nerves, no statements have as yet appeared. In grey degeneration of the cord they were found destroyed or at least rarified by Rumpf (Congress of South German Neurologists at Wildbad, May, 1878. *Centralblatt f. Nervenheilkunde*, 1878, No. 6, p. 141).

central end of the divided nerve. At the time of the section the myeline escaped from the nerve tubes, usually not further, however, than the first constriction; in fact even the interannular segment included in the section is not always completely emptied. The axis cylinders now hypertrophy and in this state show a distinct striation. The space between the axis cylinder and the sheath of Schwann is filled with drops of myeline and cells. These are partly red blood globules, probably pressed in; partly, however, wandering leucocytes. The latter are mostly surrounded by granulations of myeline and fat. Ranvier claims that they digest the myeline, in fact *eat their way*, and hence may pass upward within the sheath of Schwann, beyond the first constriction. In some instances they corrode even the axis cylinder. The changes are, therefore, not limited by the first constriction. Moreover, the axis cylinder appears hypertrophied, even beyond this point, while the nucleus and protoplasm of the next interannular segment are in a state of proliferation.

In the peripheral *end* on the other hand the axis cylinders have been destroyed, and at the end of a fortnight nothing is left but the emptied sheaths of Schwann.

The regeneration was studied by Ranvier on the pneumogastric nerve of rabbits, rats and Guinea-pigs. The animals were examined between the sixtieth and the one hundred and sixtieth day. At this time it can be observed that the central part of the nerve trunk is colored intensely black as usually by osmic acid. The central end, thickened, is lighter colored, as are also the peripheral end and the peripheral trunk of the nerve. The cicatricial portion becomes greyish from the action of osmic acid.

These different portions are next described in detail. The appearances, Ranvier divides into classes, viz.: ordinary and "bizarre," using the latter term because the phenomena are as yet beyond all explanation.

In the peripheral trunk examined about the sixtieth or seventieth day after the action of osmic acid, a large number of pale fibres, bearing nuclei, can be observed. These fibres are parallel and without anastomoses, hence, quite different from Remak's fibres. Other fibres have drops of myeline attached to them. There are, besides, regenerated fibres, with a thin coating of myeline, the entire fibre being very thin (four thousandth of a millimetre in diameter), and interannular segments very short, perhaps one hundred and fifty micromillimetres in length, while a normal segment measures about one thousand micromillimetres. A number of old sheaths of Schwann are filled with new axis cylinders, sometimes several in number, which are intertwined. Later, sometimes even at this time, new medullated fibres are found, not contained in old sheaths. They are of less than normal size, being ten micromillimetres thick, while their constrictions are three to four hundred micromillimetres apart. These tubes are often accompanied by a non-medullated or even very thin medullated fibre wound around them. Other fibres are seen

without sheath of Schwann. Frequently nerve fibres are seen to divide at the level of a constriction. Between the different fibres oval masses are found, consisting of protoplasm and myeline and containing nuclei: they are nothing but portions of degenerated nerve tubes. One form of elements is still to be mentioned. These are fibres medullated in the greater part of their course, but entirely without myeline in some places.

The cicatricial segment is formed of a number of small nerve bundles, even though the trunk may consist of a single fascicule. These smaller fascicules are enveloped by delicate endothelial sheaths—in fact, enlarged sheaths of Henle. The bundles consist of both medullated and non-medullated fibres, the former augmenting with time. The fibres are mostly very thin, and by no means all parallel. To illustrate this irregular arrangement, Ranvier refers to an instance, where the central and peripheral parts of the nerve seemed to end in free buttons, without any cicatricial segment. There was, however, between them a delicate membrane, apparently of connective tissue. But on dropping osmic acid on this membrane, fine black streaks appeared uniting the divided nerve ends. On coloring this specimen and placing it under the microscope, with due care, it was found, that the apparent membrane consisted in reality of a net-work of nerve fibres, connecting the central with the peripheral end. Similar deceptive appearances were most probably the cause of the erroneous statements of Philipeaux and Vulpian, that nerves can be regenerated without union to a central nerve end.

In the central end of the divided nerve, no degeneration proper occurs at any time. It may be said, that the efforts at regeneration commence at the moment of the section. Examined after the sixtieth day, it is found that from the old hypertrophied axis cylinders, there proceed in a peripheral direction new nerve fibres—as prolongations, so to speak. Many of these fibres are non-medullated, others possess myeline, but usually only a thin coat of it, which is sometimes interrupted.

The fibres themselves are mostly very thin, but not all alike in thickness. Frequently there proceed two or more fibres as prolongations of an original axis cylinder. Many of these fibres subdivide again, but always at a point of constriction, if they possess myeline. Often one of the new fibres is wound around a thicker one. Corresponding appearances are observed in cross-sections. In these it can be plainly demonstrated that the fibres of new formation grow into the old persisting sheaths of Schwann. Sometimes as many as twenty-five new tubes can be counted in a single dilated sheath.

Under the heading "bizarre" appearances, Ranvier describes some very strange observations. Of the thin fibres of new formation, one is often wound around the other. Sometimes several are intertwined like a cord. Again a fibre changes its direction suddenly, and coiling up itself becomes recurrent. How far it pursues this recurrent course could not be ascertained. The

strange appearances Ranvier refers to an excessive growth in an insufficient space. Another queer fact has been described by S. Mayer some years ago. Mayer claimed the occurrence of true nerve cells in the course of the regenerated fibres. Ranvier has seen similar appearances in the regenerated pneumogastric nerve. These objects appeared like bipolar cells interspersed in the course of non-medullated fibres. But, as they do not contain a nucleus, they cannot be considered as nerve cells.

A number of experiments are still mentioned by Ranvier, in which he divided a nerve at two points, leaving it, however, *in situ*. The intermediate portion was found to undergo the usual degenerative changes. These experiments were only made on warm-blooded animals.

Results of a different significance were obtained by Rumpf (III.) from double nerve section in the frog. As we have mentioned above, the axis cylinder of the excised frog's nerve is dissolved by lymph. Nevertheless a nerve-muscle preparation preserves its vitality for many hours, if kept in lymph or even in a 0.7 per cent. solution of NaCl. Hence Rumpf supposed that the connection of the nerve with the muscle preserved it from the solvent action of the lymph, in other words that the peripheral termination exerted a trophic influence as well as the central termination of the nerve. The loss of function does not occur in the frog's nerves until about the thirtieth day after their division, while lymph will dissolve the axis cylinder of the excised nerve in about seventy hours. But on dividing a frog's nerve at two points, so as to cut off the intermediate portion from both its central and peripheral termination, Rumpf found that the axis cylinders of the intermediate portion disappeared within three to four days!

The nervous distribution in the electric organ of the torpedo (T. Galvani) is next studied by Ranvier, since on account of its simplicity it can be considered a prototype of nerve terminations. The organ is described as semi-lunar in shape, consisting of a large number of pentagonal prisms, reaching from the skin of the back to the front of the animal. Each one of these prisms is divided into superimposed cases by horizontal partitions or lamellæ, the interspaces between them being filled with a gelatinous mass. After a careful historical review of the subject, R. describes his own methods of investigation. To avoid shrinkage he injects a one per cent. solution of osmic acid into the interior of the organ, thus maintaining the delicate lamellæ in their normal state of tension. The hardened object is hereupon placed into osmic acid until blackened. In rays and torpedos *the axis cylinders* as well as the myeline are blackened by osmic acid. Horizontal slices are hereupon removed with scissors and shaken in water until the lamellæ are isolated. The lamellæ are curved like the cornea, their dorsal side being convex, their ventral concave. The nerves enter on the ventral side. Examined in a drop of water with the ventral surface upwards, five different levels

are easily recognized by adjusting the microscope, viz.: 1. a plane, in which the medullated fibres are seen; 2. a lower plane in which capillaries ramify; 3. the medullated fibres dip down underneath the vessels to form a third plane; 4. a plane apparently granular, corresponding to the nerve-terminations; and 5. a plane presenting round nuclei and granules. In the first three of these planes star-shaped cells with delicate processes are found. These cells belong to the mucous tissue contained in the space between the lamellæ and filling out any interspaces existing between the nerve fibres. Certain peculiarities are found in these nerves. They divide at first dichotomously, giving off both lateral and terminal branches. They are surrounded by a delicate endothelial sheath, which, however, R., for reasons to be detailed hereafter, does not consider as the analogue of the sheath of Henle of muscular nerves. This sheath divides with the fibres. Sometimes, however, two branches are surrounded for a short distance by one sheath. The constrictions differ from other nerves, inasmuch as they are apparently stretched, *i.e.*, the constricted unmedullated space between two segments is lengthened. The axis cylinder itself is blackened by osmic acid. The sheath of Schwann is applied very closely. As the branches divide they become successively thinner, and their interannular segments shorter. R. points out at this place, that according to a definite law, the distance between the constrictions increases with the thickness of the fibres. Finally the smallest branches lose their myeline. At a point of constriction the myeline ceases to surround the nerve any further, while the sheath of Schwann and the secondary sheath continue, but are applied closer. The sheath of Schwann probably proceeds to the end of the fibre, while the secondary sheath ends abruptly in a *terminal ring*. The naked axis cylinders display in this organ a distinct fibrillary structure, particularly after the action of osmic acid or staining with gold by Gerlach's method. The places of bifurcation are usually triangular. This is due to the fact that the branches collectively contain more ultimate fibrillæ, than the original axis cylinder. Evidently fibrillæ pass from one branch into another, connecting by loops the nerve terminations. The ultimate ramification of the naked fibres has been compared by Wagner to the shape of a stag's horn.

The parts so far described are really yet on the outside (ventral surface) of the electric lamella. They are surrounded by the mucous tissue. The greatest difficulties in observation commence only in the study of the electric lamella itself, and now stronger lenses are required. Since much diversity of opinion exists as to the structure of the lamella apart from the nerve terminations, R. elucidates this point in the first place. We notice here with pleasure an illustration of Ranvier's methodic preciseness and the fine results to be obtained therefrom. The lamella, isolated after an interstitial injection of osmic acid, is macerated in a mixture of one part of alcohol to two of water. Hereupon

it is placed in a glass slide, ventral side upwards, and allowed to dry partially. Thus adherent it is immersed in alcohol and smartly brushed with a camel's-hair brush. The lamella is thus split unequally into layers, of which four can be distinguished: (1) a layer, called *nervous lamella*, consisting really of two parts, a superficial (ventral) layer containing the ultimate nerve terminations, and a deep layer composed of short *vertical* fibres (called by R. *electric cilia*) passing like a row of palisades towards the (2) *intermediate layer*. This also consists of two portions, a superficial part of a finely granular appearance, which is due to the electric cilia, and a deep layer, more coarsely granular, containing nuclei. These two layers correspond to the fourth and fifth planes recognizable by different *focal* adjustment in the surface view of the entire lamella. (3) A structureless, thin membrane, the dorsal lamella and (4) a connective layer consisting of a trellis-work of very fine connective fibres which support the entire lamella. Corresponding appearances are obtained by cross-sections.

For the study of the nerve termination three methods are recommended, the results of one supplementing and controlling the appearances furnished by the others. These are (*a*) staining with (solid) nitrate of silver, (*b*) intense coloration by osmic acid and subsequent treatment with chloride of gold and potassium (1 per cent.) and (*c*) staining with hematoxylin after preliminary injection of osmic acid. Satisfactory views are also obtained from the *fresh* lamella, but only after previous knowledge of its structure.

The different methods reveal, that the ultimate nerve fibres beyond the "stag's horn" ramification enter vertically the nervous lamella and expand here into *leaf-like terminations*, between which broad anastomoses exist. From all appearances R. concludes, that these terminations are held together by a structureless membrane, constituting the superficial layer of the nervous lamella. This membrane, which can even be isolated in small fragments, is in all probability derived from the union of the sheath of Schwann of the different fibres, since this sheath is not seen terminating at any other place. From the lower surface of the leaf-like nerve expansions the electric cilia pass like a regular row of palisades to the upper (ventral) surface of the intermediate layer. The lower portion of this layer is evidently not solid, since in the fresh specimen the coarser granules are seen to perform Brownian movements. The nuclei found in this layer possess no cell-body. R. hence considers the entire layer as the equivalent of a single cell with multiple nuclei.

The wall of the prisms of the electric organ consists of a trellis-work of connective tissue fibres. There is besides a framework running through the organ, in which the prisms are imbedded. This framework can be compared as regards its structure to the lamellar sheaths of nerve trunks. The electric lamellæ themselves are united with the wall of the prism by means of the network of connective tissue on their dorsal surface. The dorsal

surfaces of all lamellæ (of one prism) are thus mutually connected. The remaining layers of the lamella bend downward along the wall of the prism and terminate just above the dorsal surface of the next lamella.

Next in place is a study of the electric nerve fibres as they appear in the trunk. Besides the sheath of Schwann the individual fibres are surrounded by a secondary sheath, which prolongs itself, and has been described as such with the fibres ramifying in the electric organ. Its existence in the trunk establishes a difference between it and the sheath of Henle of muscular nerves, which latter is really the continuation of the lamellar sheath. The interannular segments of the electric nerves are remarkably short. Thus a fibre in the electric nerve trunk of 12 micromillimetres diameter consists of segments of 500 to 600 micromillimetres in length, while fibres from other nerves of the same animal and of the same thickness consist of segments of twice that length. This observation supports R.'s theory, that the length of space between the constrictions varies inversely with the energy of nutrition of the nerve, since, according to R., the nutritive fluids pass in and out at the constrictions where no myeline opposes their passage. At any rate R. cannot well be contradicted in asserting that the electric nerves are the most active of any nerves in the sluggish torpedo.

The trunk of the electric nerve consists, near its origin, of a few large fascicules, which increase in number and diminish in size in passing towards the periphery. R., however, has never observed any division of nerve fibres within the trunk. The nerve bundles are surrounded by sheaths passing off from the common lamellar sheath. In the electric trunk all the intrafascicular tissue presents a more distinctly lamellated arrangement than it does in nerves of other animals. In other nerves the last trace of the intrafascicular tissue appears as a sheath around the nerve fibres, consisting of sparse connective fibres. In the electric nerves, on the other hand, we find instead, a sheath around the fibres in the trunk, consisting of lamellated endothelium, *i. e.*, the secondary sheath, which continues beyond the point where the ramifying nerves lose their myeline.

A peculiar mode of nerve division is observable in the walls of the electric prism. A single nerve fibre running on the inside of the wall will subdivide into a large number (as many as 20) branches. The axis cylinder undergoes a considerable thickening at the point of a constriction and splits abruptly into many branches. In honor of the discoverer, R. calls these divisions "bouquets" of Wagner. The resulting branches exceed in thickness the original axis cylinder, probably on account of the existence of loops of fibrillæ, which do not enter the parental axis cylinder. Still this is not so demonstrable, as it is in the non-medullated branches in the electric lamella, yet it can be positively observed that the volume of the collective nerve fibres

increases from the place where they leave the trunk up to the periphery.

Ranvier enters hereupon into the physiology of the electric organ and furnishes us with a captivating hypothesis of its action. The organ is controlled by the will of the animal. In answer to a strong irritation the animal gives a severe shock. This shock, however, is composed, as Marey has shown, of a series of discharges, hence analogous to the muscular tetanus, consisting of superimposed single contractions. The shocks can be repeated, but feebler, until the animal is exhausted. Not every irritation causes a shock, unless the animal is enfeebled, when they become apparently involuntary reflexes. On laying bare the electric lobes, whence the electric nerves originate, discharges can be induced by direct irritation of the lobes. But a different result is observed when the electric nerves are divided and then irritated. *No shocks can be perceived by the hand*, although a delicate galvanometer or a sensitive nerve-muscle preparation will reveal a *very feeble* discharge following each direct irritation of the exposed and severed nerves. Boll recently stated, that the torpedo is not paralyzed by curare. R., however, found that strong doses of this poison *will* paralyze the motor nerves, without, however, impairing the activity of the electric nerves of the fish.

As a basis for his hypothesis, Ranvier reminds his readers that the electric lobes consist of nerve cells with two kinds of processes, (*a*) several short ramifying processes, (*b*) a single Deiters' process, which is prolonged as an axis cylinder. This axis cylinder continues in the trunk, until it splits in the wall of the electric prism into the bouquet of Wagner. From this point further subdivisions occur until the fibres end in the leaf-like expansion in the electric lamella. From these leaves the electric cilia proceed up to the surface of the intermediate layer. Let us suppose, that by some chemical process there occurs in the nerve cell a separation of electricity into positive and negative fluid, and that the positive electricity passes out into the branching processes. The negative electricity could in that case proceed along the Deiters' process and axis cylinder to the nerve termination and electric cilia. If now the intermediate layer is a poorer conductor than the other layers of the electric lamella, the dorsal surface will become charged with positive electricity. The dorsal surfaces of all lamellæ are in mutual connection through the walls of the prisms. The nerve terminations are also mutually connected through the nervous loops previously referred to. Hence the electric organ can be compared to a condenser or Leyden jar, which discharges itself as soon as the necessary electric tension has been attained. That the chemical processes generating the electricity do not occur in the electric organ itself, seems likely on considering the feeble blood-supply of the organ. On the other hand, their occurrence in the electric lobe is vouched for by the inability to obtain strong discharges by stimulating

the divided electric nerves. The very feeble shock which does result from the direct stimulation of the nerve, might well be caused by chemical processes in the nerve itself.—This hypothesis rests, as far as histology is concerned, on a solid basis. It certainly deserves as much credit as any explanation of this organ by other authors.

The study of nerve terminations in muscles is preceded by a thorough resumé of the structure of the muscle. It would, however, unduly lengthen this review to follow Ranvier in this matter, as well as in his historical review of the nerve terminations. Suffice it to say, that these rather obscure subjects are treated in a remarkably clear manner.

Before proceeding to the demonstration of the ultimate nerve ends, Ranvier describes the mode of division of nerves in muscles, choosing as a type the thoracic cutaneous muscle of the frog. The animal is anæsthetized and extended upon a cork plate. Hereupon half a cubic centimetre of osmic acid (1 per cent. sol.) is injected under the skin over the sternum. The thin, transparent muscle, which passes from the latter bone upwards and outwards to the skin, is hereby rendered rigid and can now be easily removed, while in the fresh state this is a very delicate procedure. In the muscle examined in its nutrient fluid, the medullated nerves are seen to enter, several in number, at the lower corner of the internal surface. The subdivisions, very numerous, always occur at a point of constriction. The minute nerve trunk is enclosed by a thin lamellar sheath, which continues finally to surround the isolated fibres as a single layer of endothelial cells —the sheath of Henle. The sheath of Schwann is so closely applied to the nerve fibre that it cannot be recognized. The fibres terminate apparently with free ends. That this is a deception can be proven by the study of other muscles.

Commencing with insects, R. opens the shell of the leg of the hydrophilus and extracts some of the muscular fibres, which are then examined in a drop of the animal's abdominal fluid. As soon as the spontaneous movements cease, the double striation of the muscular fibres can be recognized. They are surrounded by tracheæ, which appear dark on account of the inclosed air, and by nerve fibres. The latter consist of an axis cylinder, presenting a fibrillary appearance, and are surrounded by a sheath peculiar to insects. At a certain place this sheath blends with the sarcolemma, while the axis cylinder enters the eminence of Doyère. The axis cylinder splits into a bundle of fibrillæ, which surround a granular cone, continuous with a layer of protoplasm lining the inside of the sarcolemma. The fibres cannot be followed beyond the base of the cone, where a number of nuclei can be seen.

Repeating as much as possible, in his demonstrations, the historical development of the subject, Ranvier chooses as the next specimen the muscles of the thigh of the lizard, treated with HCl. one part in 1,000 water. The agent coagulates the

muscle and hence renders it opaque, but subsequently transforms the myosine into syntonine, and thus produces perfect transparency. In these preparations it can be seen that the sheath of Henle blends with the sarcolemma. It is not possible to ascertain what becomes of the sheath of Schwann. The axis cylinder cannot be followed beyond its entrance into the muscle, where it loses its myeline. Fifteen to twenty nuclei are found in the eminence, shrunken from the action of the acid.

Cohnheim's treatment with nitrate of silver is next resorted to. A fragment is taken with sharp scissors from the triceps muscle of the lizard and teased in a drop of the animal's serum. Those muscular fibres of the specimen which possess nerve terminations, visible with a low power, are transferred into a 0.2 per cent. solution of nitrate of silver. After ten to twenty seconds sojourn they are washed in distilled water and exposed to daylight. When browned by light they are transferred into dilute acetic acid (one per cent.) in which they regain their normal dimension after shrinking in the silver solution. They are now examined in a mixture of glycerine and water. By this procedure the living muscular fibres are stained brown, but on the surface only, while the portions underneath the nerves present a white negative image. It is thus seen that the nerve fibre divides, and that its branches subdivide still further, in a manner comparable to the branches of a tree (*arborisation*).

Supplementary positive images, in which the nerves are colored, while the muscle is pale, are obtained by staining with gold. Ranvier recommends for this Löwit's method, consisting in the successive treatment by formic acid (one in three), chloride of gold (one in one hundred), and again formic acid. Like all gold staining, the method is not always a success. The branching violet nerve fibres are seen to end in broad expansions. By the action of the formic acid, branches are often torn between a larger stem and the terminal expansion. The gold staining reveals sometimes a granular appearance surrounding the nerve branches.

Kühne, in a recent article (in *Untersuchungen aus dem phys. Institut Heidelberg*), claims, that during life anastomoses exist between the terminal expansions, which are but poorly shown by Löwit's method, on account of the rents produced by formic acid.

The intravaginal net-work of the muscle shown by gold staining, which Gerlach claims to be connected with the nerve, in fact, its termination, is altogether contested by Ranvier. According to him it is only a protoplasmic net-work studded with fat granules, and has nothing to do whatever with the nerve.

Further details are revealed by interstitial injections of osmic acid, followed by staining with picrocarmine. Cross-sections of muscle and eminence are also described by Ranvier. The results thus obtained are compared with the fresh specimen. Ranvier also mentions a procedure by which he succeeded in preserving

the appearances of the fresh specimen. It consists in adding one part of alcohol in two parts of water on the glass slide.

From these different methods, applied to the muscles of the lizard and snake, the following results are obtained. The axis cylinder of the medullated nerve enters the muscle at the nerve eminence. At this point the myeline ends in a constriction, while the sheath of Henle blends with the sarcolemma. Sometimes the nerve branches immediately before it enters the muscle. The naked axis cylinder branches after entering the eminence, and ends finally with broad expansions. The anastomoses between the branches, which Kühne describes, Ranvier claims not to have seen. He refers them rather to the overlapping of branches. A granular *sole* at the base of the eminence does not exist, in reality the individual branches are surrounded by a hazy substance. Three kinds of nuclei are found in the eminence, (*a*) small, flat nuclei, strongly colored by picrocarmine, lining the membrane covering the eminence, hence really belonging to the sheath of Henle, and called by Ranvier *vaginal nuclei;* (*b*) large, oval, double-contoured nuclei, with brilliant nucleoli—they are faintly colored by picrocarmine and are situated at the base of the eminence (*fundamental nuclei;*) and (*c*) nuclei intermediate between these two varieties in size and coloration, situated between the nerve branches — *nuclei of nerve branches* (noyaux de l'arborisation).

Ranvier refers to some microscopic observations of curarized muscles, which did not differ from normal objects. Kühne, however, in his last memoir (*Untersuchungen, etc.*, Heft II., Bd. II., p. 208) claims to be able to distinguish between normal nerve terminations and those of lizards poisoned with *large* doses of curare. In the latter case the details of the branches appear more marked within the first hour after death than they do normally. During life no details can be recognized at all, all parts appearing homogeneous. It is only after excision of the muscular fibre that the details begin to appear gradually. According to Kühne the distinctness of the nerve eminence is so far in advance, in strongly curarized muscles, that a difference can be recognized.

In mammals the nerve terminations resemble those of the lizard, but are crowded into a somewhat smaller space.

In the frog the arrangement is somewhat different. The form of the branches resembles a bush, to which it has been compared by Kühne. The nerve fibres divide into several medullated branches applied to the sarcolemma like the extended fingers of a hand to the surface of a cylinder. Thence naked fibres pass underneath the sarcolemma and continue to branch, maintaining on the whole the form of a bush, with rather long branches, the ends of which are not broadened. Neither a granular substance nor fundamental nuclei are found, while the other varities of nuclei are similarly arranged as in lizards.

No method has as yet revealed any nerve prolongation beyond

the apparent ends of the branches, hence we are justified in considering them the real nerve terminations.

The last pages of the book detail three observations made after the section of the sciatic nerve of rabbits. It was found that the degenerative changes, especially the fragmentation of the myeline, occurred earlier in the nerves near their termination than in the trunk. Ranvier seeks the cause in the shortness (and thinness) of the interannular segments, at the periphery of the nerve; since the changes depend on the activity of the cellular elements, they must progress the more rapidly the more there are of them in a given length. Probably there exist also differences in the nutritive supply of the nerve in the trunk and in the periphery. Twenty-four hours after the nerve section the nuclei of the nerve eminence were found enlarged, proving that they participate in the exaggerated activity of the protoplasm and nuclei of the nerve itself.

The object of this review was to abstract mainly those original observations, which have not yet passed into current literature. But apart from the wealth of new discoveries, the book is a mine of information both as to modes of research, and the results obtained. The style could not be excelled in clearness, and the plates, corresponding faithfully to the original slides, as the writer can testify, deserve the same praise. Perhaps the gravest fault to be found in the work is the scarcity of microscopic measurements.

H. GRADLE.

IV.—LOCALIZATION IN BRAIN DISEASE.

LECTURES ON LOCALIZATION OF DISEASES OF THE BRAIN. By J. M. Charcot. Edited by Bourneville. Translated by Edward P. Fowler, M. D., New York. William Wood & Co., New York, 1878. Pp. 133.

This attractive little volume, composed of twelve lectures, introductory to his course in the faculty of medicine in Paris, are by the distinguished chief of the division for nervous affections, at the Salpêtrière—Professor Charcot. They have been already published, in part at least, in the *Progrès Médical*, a Parisian journal edited by Dr. Bourneville (a pupil of Charcot), who charged himself with the duty of reporting and publishing them in France. These lectures were delivered at the opening of the course of instruction of the past year, and now appear for the first time in the English language.

Dr. Charcot is well known everywhere, among those interested in the study of nervous diseases, or who have at heart the true interests of scientific medicine. He is a good example, among living physicians, of a well balanced investigator, fairly